IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

ABBOTT GMBH & CO., KG, ABBOTT BIORESEARCH CENTER, INC., and ABBOTT BIOTECHNOLOGY LTD.,	)	C.A. No. 4:09-CV-11340 (FDS)
Plaintiffs,	)	JURY TRIAL DEMANDED
v.	)	
CENTOCOR ORTHO BIOTECH, INC. and CENTOCOR BIOLOGICS, LLC,	)	
Defendants.	)	

CENTOCOR'S MEMORANDUM
ON THE ISSUE OF WILLFUL INFRINGEMENT

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The Centocor defendants submit this brief regarding Abbott's claim that Centocor has willfully infringed Abbott's asserted patent claims.

The first prong of the willfulness determination requires Abbott to prove, by clear and convincing evidence, that Centocor acted despite an objectively high likelihood that its actions constituted infringement of a valid patent. *In re Seagate Technology, LLC,* 497 F.3d 1360, 1371 (Fed. Cir. 2007) (en banc). The Federal Circuit's recent *Bard* case held that this prong is a "threshold" question that must be determined by the court and not the jury. *Bard Peripheral Vascular, Inc. v. W.L. Gore & Assoc., Inc*., 682 F.3d 1003, 1006-07 (Fed. Cir. 2012).

As set forth in Centocor's pre-trial briefing on willful infringement (D.I. 420 and 449) and in submissions during the course of this trial (D.I. 457), Abbott cannot satisfy this threshold question because Centocor's defenses are credible and reasonable. *Spine Solutions, Inc. v. Medtronic Sofamor Danek USA, Inc.*, 620 F.3d 1305, 1319 (Fed. Cir. 2010); *Black & Decker, Inc. v. Robert Bosch Tool Corp.*, 260 Fed. Appx. 284, 291 (Fed. Cir. 2008) (unpublished) (Ex. 1); *LG Display Co., Ltd. v. AU Optronics Corp.*, 722 F. Supp. 2d 466, 471 (D. Del. 2010). The determination of whether Centocor's defenses are reasonable must be made by the Court based on all the record evidence, including evidence submitted at trial. *Bard Peripheral*, 682 F.3d at 1008 (reasonableness of the defense should be determined based on the record ultimately made at trial). Importantly, it matters not that the jury has not rendered a verdict in this case. Nor does it matter what jury verdict is ultimately returned. If Centocor's defenses are reasonable, which they are, they are reasonable whether or not the defenses are ultimately successful.[1]

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[1] *See, e.g., Astrazeneca AB v. Apotex Corp.*, 2010 U.S. Dist. LEXIS 58044, *19-21 (S.D.N.Y. June 8, 2010) (granting motion for judgment as a matter of law of no willfulness because defendant "raised legitimate, substantial questions of non-infringement" despite not ultimately succeeding at trial) (Ex. 2); *Honeywell Int'l. Inc. v. Universal Avionics Sys. Corp.*, 585 F. Supp. 2d 636, 644 (D. Del. 2008) (granting summary judgment of no willfulness because defendant presented "substantial" and "reasonable" invalidity defenses requiring an "exhaustive analysis"

It is only after Abbott proves, by clear and convincing evidence, that Centocor acted despite an objectively high likelihood that the asserted claims were both valid and infringed, that the second prong of the *Seagate* test for willfulness is implicated. This second prong is directed to the issue of whether the objectively defined risk was either known or so obvious that it should have been known to Centocor. *Seagate*, 497 F.3d at 1371. It is only after Abbott has satisfied the first objective prong that Centocor's subjective state of mind becomes relevant. *Id.*

The substantial evidence that was presented to the jury during the liability phase – outlined below – establishes the credibility and reasonableness of Centocor's defenses. Because Abbott has not met the threshold question of objective reasonableness and the potential prejudice to Centocor (*see, e.g.,* D.I. 420, 449, 457), allowing the jury to hear evidence of Centocor's alleged subjective state of mind would prejudice Centocor in the eyes of the jury. The Court should, therefore, grant JMOL of no willful infringement before the damages phase of this trial, if there is one. Otherwise, the only way to avoid unfair prejudice to Centocor during the damages phase of the trial would be to trifurcate the issue of willfulness for a third trial phase.

I. CENTOCOR'S WRITTEN DESCRIPTION DEFENSE IS OBJECTIVELY REASONABLE

Centocor's written description defense is objectively reasonable.

The written description requirement is only satisfied if a person of ordinary skill in the art, reading the patent specification at the time it was filed, would recognize that it described the invention as claimed and that the inventor possessed *the full scope* of the invention as claimed. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344-47 (Fed. Cir. 2010) (en banc). The

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by the court even when those defenses did not ultimately prevail); *ResQNet.com, Inc. v. Lansa, Inc.*, 533 F. Supp. 2d 397, 420 (S.D.N.Y. 2008) (overruled on other grounds) (finding that "[w]hile [defendant] was ultimately unsuccessful [with its invalidity and noninfringement defenses], its arguments in these areas were substantial, reasonable, and far from the sort of easily-dismissed claims that an objectively reckless infringer would be forced to rely upon").

claims of the asserted patents claim antibodies by their function (e.g., binding to IL-12, neutralizing IL-12, having a particular affinity, etc.) rather than by their structure. The *Ariad* court noted the following with respect to functionally-defined genus claims:

> [A] generic claim may define the boundaries of a vast genus of chemical compounds, and yet the question may still remain whether the specification, including original claim language, demonstrates that the applicant has invented species sufficient to support a claim to a genus. *The problem is especially acute with genus claims that use functional language to define the boundaries of a claimed genus.* In such a case, the functional claim may simply claim a desired result, and may do so without describing species that achieve that result. But the specification must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus.

Id. at 1349 (emphasis added).

Ariad held that, in the case of genus claims, "the disclosure [must be] of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Id.* at 1350 (citing *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568-69 (Fed. Cir. 1997)). Because there is no dispute that the Abbott patents fail to disclose common structural features for the members of the genus they claim (D.I. 341 at 40), the written description issue here centers on whether Abbott's patents disclose a representative number of species falling within the scope of the claimed genus. It is not just the *number* of disclosed species disclosed that is relevant. As the Court noted in its Amended Memorandum and Order on Cross-Motions for Summary Judgment (*id*. at 43), where there is a substantial variation within the members of a claimed genus, the patent must describe a *sufficient variety* of species to reflect that variation. *Carnegie Mellon Univ. v. Hoffman-La Roche, Inc*., 541 F.3d 1115, 1124 (Fed. Cir. 2008) (citation omitted).

Centocor's written description defense is objectively reasonable. There is substantial evidence of the variability within the genus covered by Abbott's asserted claims, which cover antibodies as different as J695 and Stelara. There is also substantial evidence that the Joe 9 family of antibodies described in the patents are not representative of the variety of species within the genus. Specifically, the evidence shows, among other things, that:

- Stelara and the Joe 9 antibodies bind to IL-12 at different places (Day 3 Tr. at 144:21 – 145:12; Day 4 Tr. at 76:24 – 77:10, 83:7-25).
- Because of the different binding region, Stelara and J695 have different biological properties (Day 5 Tr. at 20:1 – 21:3).
- Looking at the dozens of contacts that Stelara makes with IL-12 and at the dozens of contacts that J695 makes with IL-12, not one of them is the same at a chemical and structural level (Day 3 Tr. at 161:2-24).
- Structural information about J695 binding to IL-12 was kept confidential by Abbott (*id*. at 155:3-22).
- The amino acid sequence of Stelara and J695 are about 50% different, and antibodies more structurally similar to J695 bind to completely different targets (Day 4 Tr. at 33:9 – 34:19).
- The only antibody sequences described in the Abbott patents are in the Joe 9 lineage (Day 5 Tr. at 16:25 – 17:3) and there is only about a 10% difference among the sequences of all of the Joe 9 lineage antibodies in the patents (*id*. at 24:24 – 25:3).
- The lengths of the CDR3 regions in Stelara and J695 are different (Day 4 Tr. at 32:6-16). It is the combination of the six CDRs – the three heavy chain CDRs and the three light chain CDRs – that together make the binding region to direct the antibody to a particular binding site on IL-12 (*id*. at 31:10-25).
- There is no way to predict what will happen to an antibody's function if even a single amino acid in the antibody sequence is changed (Day 5 Tr. at 25:13-16).
- Based on what is described in the patents, there is no way to predict the amino acid sequence of an antibody falling within the scope of the asserted claims (*id*. at 26:8-15).
- The heavy chain of Stelara is in the VH5 family, but all of the antibodies disclosed in the Abbott patents are in the VH3 family (*id*. at 35:8 – 36:14).
- The light chain of Stelara is in the kappa family, but all of the antibodies described in the Abbott patents are in the lambda family (*id*. at 36:22 – 39:1).

Dr. Siegel testified that the only antibody sequences described in the Abbott patents – the Joe 9 lineage – are not representative of the genus of antibodies covered by the scope of the Abbott patent claims (*id*. at 39:23 – 40:1). He also testified that, from the perspective of the person of ordinary skill in the art, the patents do not provide a description showing that the inventors possessed an invention that was broad enough to encompass a group of antibodies that includes Stelara (*id*. at 40:2-8). Dr. Marks admitted that, based on the information that is given in the patents, you cannot visualize the amino acid sequences for the antibodies that will be encompassed within the claims that are not within the Joe 9 lineage (Day 9 Tr. at 142:21 – 143:1); *see Ariad*, 598 F.3d at 1350 ("the disclosure [must be] of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." (internal citation omitted)).

Importantly, the meaningful structural and functionally differences between Stelara and the Joe 9 antibodies show that there is wide variation within the claimed genus and that the Joe 9 antibodies are not representative of the varied species in that genus. Centocor's written description defense is reasonable based on all the record evidence, including evidence submitted at trial.

II. CENTOCOR'S ENABLEMENT DEFENSE IS OBJECTIVELY REASONABLE

Centocor's enablement defense is also objectively reasonable.

To meet the enablement requirement, a patent specification "must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (internal quotation marks omitted). Although a specification need not disclose what is well known in the art, it "must supply the novel aspects of an invention in order to constitute adequate

enablement." *Id.* at 1366; *see also Auto. Techs. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1283 (Fed. Cir. 2007) ("Although the knowledge of one skilled in the art is indeed relevant, the novel aspect of an invention must be enabled in the patent."). Indeed, the Federal Circuit has made clear that a patentee cannot rely solely on the level of skill in the art to enable the novel aspects of the claimed invention. *Genentech*, 108 F.3d at 1366; *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1329 (Fed. Cir. 2009) ("[T]he proper focus when assessing enablement is on what is disclosed in the patent, not what is taught in the prior art.").

The Abbott patents must enable at least one method for making the full scope of antibodies covered by the claims. As the Federal Circuit explained in the *Genentech* case, the specification must "supply the novel aspects of an invention in order to constitute adequate enablement," and that disclosure includes providing specific starting materials. *Genentech*, 108 F.3d at 1366. Otherwise, undue experimentation would be required to practice the claimed invention. *Id.* The following evidence shows that the Abbott patents fail to give that disclosure.

The scope of the claimed invention includes antibodies with a VH5 heavy chain – antibodies like Stelara (Day 5 Tr. at 36:2-5). The patents describe using the Vaughan phage display library to make antibodies of the invention (*id.* at 43:22 – 45:7), but the Vaughan publication cited in the patent shows only VH1, VH3, and VH4 antibodies coming out of that library (*id.* at 44:10-25), and specifically does not provide any examples of antibodies that came from a VH5 family (*id.* at 44:8-25; Day 9 at 93:17 – 94:23). Dr. Siegel has testified that the patents do not enable making an antibody with a VH5 heavy chain from a phage library (Day 5 Tr. at 45:1-7).

Dr. Marks has not contradicted Dr. Siegel's testimony about what the Vaughan reference says, but has suggested a legally erroneous standard for assessing enablement. Dr. Marks has

testified that a person of ordinary skill could use the sequences disclosed in the patents to make antibodies within the scope of the claims and that is, in his opinion, sufficient (Day 9 Tr. at 111:1-9). But enablement requires enabling more than the sequences disclosed, it requires enablement for the full scope of the claim, which is not limited by any sequences. *Genentech*, 108 F.3d at 1365.

Even if VH5 antibodies could be made using transgenic mice, both Dr. Siegel and Abbott's expert Dr. Davis agree that the Abbott patents fail to teach the person of ordinary skill in the art how to use those mice to make any IL-12 antibodies (Day 5 Tr. at 45:10-47:1; Day 7 Tr. at 146:17 – 147:5). Importantly, while transgenic mouse methods were available in 1999 to make VH5 antibodies, Abbott's specification teaches nothing about transgenic mice. That is not enough, because it is the ***specification*** that must provide the enabling disclosure – not the prior art. *Genentech*, 108 F.3d at 1366 (application, not third party art, "must supply the novel aspects of an invention in order to constitute adequate enablement"); *Auto Techs. Int'l, I*, 501 F.3d at 1283 ("[a]lthough the knowledge of one skilled in the art is indeed relevant, the novel aspect of an invention must be enabled in the patent"); *ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 940-41 (Fed. Cir. 2010) (one "cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification," rather "the rule that a specification need not disclose what is well known in the art is merely a rule of supplementation, not a substitute for a basic enabling disclosure").

Centocor's enablement defense is reasonable based on all the record evidence, including evidence submitted at trial.

III. CENTOCOR'S PRIOR INVENTION DEFENSE FOR THE "COMPOSITION" CLAIMS IS OBJECTIVELY REASONABLE

Centocor's prior invention defense for the "composition" claims is objectively reasonable. The composition claims here are claim 64 of the 128 patent and claim 11 of the 485 patent.

Centocor contends that the composition claims are invalid under 35 U.S.C. §102(g)(2) because, for claims 64 and 11, Centocor inventors made the invention before Abbott.

Centocor scientists made and characterized the Stelara antibody, tested it to confirm that it was a human antibody (Day 3 Tr. at 32:2 – 39:15), that it bound to IL-12 (*id*. at 39:16 – 41:7), and that it neutralized IL-12 (Day 2 Tr. at 100:21 – 105:4; Day 3 Tr. at 80:18 – 82:18; 84:9 – 89:10). Dr. Ghrayeb testified that Stelara was made as a pharmaceutical composition by no later than October 1, 1997 (Day 2 Tr. at 95:5 – 100:12). Ms. Giles-Komar, one of the Stelara inventors, testified that she recognized all of these properties by no later than February 18, 1998 (Day 3 Tr. at 80:18 – 82:18; 84:9 – 89:10). She therefore appreciated that the Stelara antibody worked for its intended purpose – binding to and neutralizing IL-12.

Abbott, on the other hand, has not proved an invention date for the composition claims prior to August 1998. One of the inventors of the composition claims, Stuart Friedrich, did not start collaborating with his co-inventors on the IL-12 project until August 1998, and the law is clear that there *cannot* be a date of invention (i.e., conception) for the a joint invention any earlier than the date of inventive contribution of *all* joint inventors.

"Conception . . . is the completion of the mental part of invention." *Burroughs Wellcome Co. v. Barr Labs.*, 40 F.3d 1223, 1227-28 (Fed. Cir. 1994). Conception is also the touchstone to determining inventorship. *Fina Oil & Chem. Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997). Each person named as a joint inventor must have contributed to the conception of the invention.

Vanderbilt Univ. v. ICOS Corp., 601 F.3d 1297, 1303 (Fed. Cir. 2010). Thus, a joint invention cannot have been made – i.e., cannot have been conceived of – until each of the joint inventors has contributed to the conception of the invention. *Perkins v. Engs*, 118 F.2d 924, 928 (C.C.P.A. 1941) (question of priority of joint invention must be determined from the beginning of the joint activities of the inventors); *Samson v. Crittenden*, 1989 Pat. App. LEXIS 25, *11 (B.P.A.I. Sept. 27, 1989) ("Since Mar did not become involved with the project until late November 1984, only activities which occurred after that time may be relied upon by Samson et al. to establish joint conception and reduction to practice on their behalf") (Ex. 3).

Abbott has asserted, and Centocor has not disputed, that Mr. Friedrich is an inventor on all composition claims asserted by Abbott (Day 6 Tr. at 69:13-22). It is also undisputed that Mr. Friedrich did not begin working on the IL-12 project until August 1998 (Trial Ex. 2011 at 2 ("Q. What was your next job? A. My next job was with Genetics Institute. Q. And what year did you start there? A. In 1998, August of 1998, I believe."). Mr. Friedrich, therefore, could not have made his contribution to the conception of the composition claims until at least August 1998. Because an invention requires a complete conception, the composition claims could not have been conceived prior to August 1998.

Centocor's prior invention defense is also reasonable based on all the record evidence, including evidence submitted at trial.

IV. CENTOCOR'S OBVIOUSNESS DEFENSE IS OBJECTIVELY REASONABLE

Finally, Centocor's obviousness defense is objectively reasonable.

Centocor contends that all of the asserted patent claims are invalid as obvious under 35 U.S.C. § 103. The alleged invention of Abbott's claims is nothing more than a predictable variation of the prior art – i.e., it is a combination of familiar elements according to known methods which does no more than yield predictable results.

A patent is invalid "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a). The Supreme Court's landmark obviousness decision, *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), "repudiated as 'error'" the Federal Circuit's previous "restriction[s] on the ability of a skilled artisan to combine elements within the scope of the prior art." *In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009). "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." *KSR*, 550 U.S. at 421. "If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." *Id*.

The Abbott claims are obvious, based on at least the following evidence:

- As of March 1999, scientists were motivated to make IL-12 antibodies because it was generally known that excess IL-12 could lead to autoimmune diseases and because treatment of such diseases by administration of humanized antibodies had already been disclosed in the art (Day 5 Tr. at 49:14 - 51:24).

- As of March 1999, neutralizing antibodies that bound to the p40 subunit of IL-12 were known (*id*. at 52:6 – 53:14).

- As of March 1999, human antibodies to IL-12 had been isolated from some patients (*id*. at 53:15 – 55:15).

- As of March 1999, scientists knew how to use transgenic mice to make human antibodies to human antigens, and those antibodies had k_{off} rate constants meeting the claim limitations (*id*. at 58:9 – 63:6).

- As of March 1999, publications disclosed that human antibodies to human IL-12 could be made using transgenic mouse technology (*id*. at 63:7 – 67:2).

- As of March 1999, the person of ordinary skill in the art could have predicted that human antibodies within the scope of the claims could be made using transgenic mice (*id*. at 67:3-11).

- As of March 1999, the prior art disclosed phage display techniques for making high affinity, neutralizing human antibodies to human proteins, such as IL-12 (*id*. at 67:24 – 77:9).

- As of March 1999, the prior art disclosed making pharmaceutical compositions of antibodies, including compositions of antibodies in saline (*id*. at 50:23 – 51:9).

- Based on the state of the art in March 1999, it was predictable that a human antibody or pharmaceutical composition within the scope of the claims could be obtained using known techniques (*id*. at 77:10 – 81:18).

Centocor's obviousness defense is reasonable based on all the record evidence, including evidence submitted at trial.

V. CONCLUSION

The standard for willful infringement requires clear and convincing evidence of objective recklessness on the part of Centocor. Centocor has raised credible and legitimate defenses at trial, including written description, enablement, prior invention, and obviousness of the asserted claims. Abbott cannot prove the objective recklessness prong of the willfulness inquiry. Therefore, in order to comply with the Federal Circuit's holding in *Bard* and to avoid potential prejudice to Centocor during the damages portion of the trial, the Court should grant JMOL of no willfulness prior to the damages trial.

Date: September 24, 2012 By: _Dianne Elderkin___

Dianne B. Elderkin (pro hac vice)
delderkin@akingump.com
Barbara L. Mullin (pro hac vice)
bmullin@akingump.com
Steven D. Maslowski (pro hac vice)
smaslowski@akingump.com
Angela Verrecchio (pro hac vice)
averrecchio@akingump.com
Matthew A. Pearson (pro hac vice)
mpearson@akingump.com

AKIN GUMP STRAUSS HAUER & FELD LLP
Two Commerce Square
2001 Market Street, Suite 4100
Philadelphia, PA 19103-7013
215-965-1200
FAX: 215-965-1210

Emily C. Johnson (pro hac vice)
johnsone@akingump.com
AKIN GUMP STRAUSS HAUER & FELD LLP
Robert S. Strauss Building
1333 New Hampshire Avenue N.W.
Washington, DC 20036

Heather B. Repicky (BBO # 663347)
NUTTER MCLENNEN & FISH LLP
World Trade Center West
155 Seaport Boulevard
Boston, MA 02210
617-439-2000
FAX: 617-310-9000

Attorneys For Defendants
CENTOCOR ORTHO BIOTECH, INC. and
CENTOCOR BIOLOGICS, LLC

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a true and correct copy of the foregoing was served by hand on counsel for Abbott on September 24, 2012 and filed electronically through the ECF system on September 25, 2012.

/s/Angela Verrecchio_____